40 CFR Parts 798 and 799

[OPTS-42073] TSH-FRL 2906-9]

2-Mercaptobenzothiazole; Proposed Test Rule

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: The EPA is proposing that manufacturers and processors of 2-mercaptobenzothiazole (MBT; CAS No. 149-30-4) be required, under section 4 of the Toxic Substances Control Act (TSCA), to perform testing for persistence and mobility, chronic aquatic toxicity, pharmacokinetics, developmental toxicity, reproductive toxicity, neurotoxicity, and chromosomal aberrations. This proposed rule is in response to the Interagency Testing Committee's (ITC's) designation of MBT for priority consideration for chemical fate and environmental effects testing.

DATES: Submit written comments on or before January 6, 1986. If persons request an opportunity to submit oral comment by December 23, 1985, EPA will hold a public meeting on this rule in Washington, D.C. For further information on arranging to speak at the meeting see Unit VIII of this preamble.

ADDRESS: Submit written comments, identified by the document control number (OPTS-42073), in triplicate to: TSCA Public Information Office (TS-793), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm. E-108, 401 M. St., SW., Washington, D.C. 20460.

A public version of the administrative record supporting this action (with any confidential business information deleted) is available for inspection at the above address from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT: Edward A. Klein, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-543, 401 M St., SW., Washington, D.C. 20460. Toll free: (800-424-9065). In Washington, D.C.: (554-1404). Outside the USA: (Operator—202-554-1404).

SUPPLEMENTARY INFORMATION: EPA is issuing a proposed test rule under section 4(a) of TSCA in response to the ITC's designation of MBT for chemical fate and environmental effects testing consideration.

I. Introduction

A. ITC Recommendation

TSCA (Pub. L. 94-469, 90 Stat. 2003 *et seq.*; 15 U.S.C. 2601 *et seq.*) established the Interagency Testing Committee (ITC) under section 4(e) to recommend to EPA a list of chemicals to be considered for testing under section 4(a) of the Act.

The ITC designated MBT (CAS No. 149-30-4) for priority consideration in its 15th Report submitted to EPA on November 6, 1984. The report was published in the **Federal Register** of November 29, 1984 (49 FR 46931). The ITC recommended that MBT be considered for chemical fate testing, including dissociation constant; persistence in water and soil, and leaching and migration; and for environmental effects testing, including acute and chronic toxicity to fish, aquatic invertebrates and plants, and terrestrial plants. The bases for these recommendations were as follows: (1) Annual production of 2,328,000 pounds of MBT, 40,000,000 pounds of the sodium salt of MBT (NaMBT) and 4,000,000 pounds of the zinc salt (ZMBT); (2) expected environmental releases from manufacture and processing; (3) available data which demonstrate that MBT and its sodium salt exhibit high acute toxicity to aquatic organisms; and (4) expected widespread terrestrial exposure along roadways. No health effects testing was recommended because of the extensive toxicological testing of MBT already completed and currently underway.

B. Test Rule Development Under TSCA

Under section 4(a) of TSCA, EPA shall by rule require testing of a chemical substance or mixture to develop appropriate test data if the Administrator finds that:

(A)(i) the manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, may present an unreasonable risk of injury to health or the environment,

(i) there are insufficient data and experience upon which the effects of such manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data; or

(B)(i) a chemical substance or mixture is or will be produced in substantial quantities,

and (I) it enters or may reasonably be anticipated to enter the environment in substantial quantities or (II) there is or may be significant or substantial human exposure to such substance or mixture.

(ii) there are insufficient data and experience upon which the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data.

EPA uses a weight-of-evidence approach in making a section 4(a)(1)(A)(i) finding: both exposure and toxicity information are considered in determining whether available data support a finding that the chemical may present an unreasonable risk. For the finding under section 4(a)(1)(B)(i), EPA considers only production, exposure, and release information to determine whether there is or may be substantial production and significant or substantial human exposure or substantial release to the environment. For the findings under sections 4(a)(1)(A)(ii) and (B)(ii), EPA examines toxicity and fate studies to determine whether existing information is adequate to reasonably determine or predict the effects of human exposure to, or environmental release of, the chemical. In making the finding under section 4(a)(1)(A)(iii) or (B)(iii) that testing is necessary, EPA considers whether ongoing testing will satisfy the information needs for the chemical and whether testing which the Agency might require would be capable of developing the necessary information.

EPA's process for determining when these findings apply is described in detail in EPA's first and second proposed test rules as published in the Federal Register of July 18, 1980 (45 FR 48524) and June 5, 1981 (46 FR 30300). The section 4(a)(1)(A) findings are discussed at 45 FR 48524 and 46 FR 30300, and the section 4(a)(1)(B) findings are discussed at 46 FR 30300.

In evaluating the ITC's testing recommendations concerning MBT, EPA considered all available relevant information including the following: Information presented in the ITC's report recommending testing consideration and any public comments on the ITC's recommendations; production volume; use, exposure, and release information reported by manufacturers of MBT under the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712); health and safety studies submitted under the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR Part 716) concerning MBT; and published and unpublished data available to the Agency. Based on its evaluation, as described in this proposed rule, EPA is proposing chemical fate and health effects testing requirements for MBT under section 4(a)(1)(B), as well as environmental effects testing of MBT under section 4(a)(1)(A) and (B) of TSCA. By this action, EPA is responding to the ITC's designation of MBT for priority testing consideration.

II. Review of Available Data

A. Profile

MBT is a yellow solid with a disagreeable odor, melting at 177–178 °C (Ref. 1). The calculated water solubility is 51 mg/l at pH 5, 118 mg/l at pH 7, and 900 mg/l at pH 9 (Ref. 2). It has a vapor pressure of 1.9×10^{-4} at 25 °C (Ref. 2) and an experimentally derived dislocation constant of 6.93 (Ref. 3). The octanol/water partition coefficient has been estimated to be 1.61 (Ref. 4) and measured to be 2.24 (Ref. 2).

B. Production

The major manufacturers of MBT are B.F. Goodrich Co., Goodyear Tire and Rubber Co., Monsanto, and Uniroyal Chemical Co. (Ref. 19).

MBT is manufactured by the reaction of aniline with equimolar quantities of sulfur and carbon disulfide at 250 °C and 450 psi in a continuous closed process at high pressure. Purification can be accomplished by dissolving in aqueous base, followed by representation in acid (Refs. 5 and 6).

The 1984 MBT production volumes have been submitted to the Agency as confidential business information (CBI). The 1981 production volume of MBT was reported to be 2,328,000 lbs (Ref. 7). The 1983 sales volume was reported to be 5,958,000 lbs (Ref. 9).

Indirect production of MBT can result during the vulcanization process from the breakdown of MBT-derived accelerators (Ref. 8).

C. Use

MBT is used mainly as a vulcanization accelerator in rubber manufacture and as an intermediate in the production of other accelerators. Vulcanization involves the formation of sulfur bridges which crosslink rubber polymers. Vulcanization accelerators cause the crosslinking to occur at lower temperatures and shorter curing times than would be otherwise required, resulting in a product with more uniform and predictable properties. MBT is an accelerator with little if any delay in its curing time (Ref. 8). Because of its high activity, MBT has become more of a specialty accelerator for products such as shoe soles requiring fast curing at low temperture. However, MBT is extensively used as an intermediate to produce other rubber accelerators of which decompose during vulcanization to release MBT (Ref. 19).

Secondary uses of MBT includes use as a corrosion inhibitor in cutting oils and petroleum products (Ref. 10), and as a fungicide in clothing for use in the tropics (Ref. 11).

D. Exposure and Release

1. *Occupational.* The National Occupational Hazard Survey (NOHS) data base (Ref. 12) estimates that as many as 558,893 people in the chemical industry may be exposed to MBT. The National Occupational Exposure Survey (NOES) data base (Ref. 13) estimates that 2,398 workers (of whom 119 are female) are exposed to MBT. The NOHS data base reports actual exposures, exposure to trade name products though to contain MBT, and exposure to products of the type that contain MBT. The NOES data base is limited to workers present where MBT has been identified to be present. Uniroyal has estimated that up to 15 workers may be involved in direct production of MBT for about 20 percent of their work-year (Ref. 14). Worker exposue may be limited by the closed manufacturing system, unpleasant odor, potential for production of allergic dermatitis, and the regulatory need to limit exposure to reactants such as aniline. Beside worker exposure to MBT during production, exposure to MBT is possible during rubber manufacture (Ref. 15), cleaning of manufacture vessels (Ref. 16), drying and grinding (Ref. 10), handling and emptying bags used to transport MBT (Ref. 17), contact with waste waters (Ref. 18), rubber reclaiming, tire recapping, tire burning, and contact with MBT compound containing materials (Ref. 11).

2. *Consumer and general population.* Consumer exposure to MBT could be extensive as a result of its presence in finished rubber goods and the ubiquitous presence of rubber in manufactured consumer items. In the past, allergic dermatitis has been traced to MBT incorporated in clothing articles, i.e., shoes and elastics, and other rubber products contacting human skin (Ref. 19, 54 through 58).

Several products under Food and Drug Administration jurisdiction have been shown to contain residual MBT. This information provides evidence that residual MBT can be present in vulcanized rubber products after processing and leads EPA to conclude that MBT may similarly be present in

vulvanized rubber products under TSCA jurisdiction. MBT has been shown to leach out of several commercial products including the stoppers of 500-ml infusion bottles, single-dose injection syringes, rubber baby bottle nipples, and rubber articles for food contact. The concentrations found in the single-dose injection syringes ranged from 0.7 to 2.0 ppm (Ref. 20). MBT was detected in the aqueous extracts of rubber baby bottle nipples at a mean concentration of 3 ppm, with some samples reaching 30 ppm (Ref. 21). Rubber products in contact with food showed MBT concentrations of 12.3 to 85.8 ppm when run through a series of extractions (Ref. 22).

Human exposure to MBT in ambient air has been estimated from modeling using 2,2'-dithiobis(benzothiazole) (MBTS) and an air dispersion model. EPA estimated air concentrations of MBTS within 1,000 meters of an elastomer manufacturing site to be 0.01 mg/m^3, equivalent to an inhalation exposure of 0.035 mg/kg body weight/day (820 mg/year). This estimated value probably approximates that for MBT (Ref. 23).

3. *Environmental.* Environmental exposure to MBT results from several sources. The greatest potential for the exposure of nonhuman populations to MBT is to the aquatic environments receiving waste water from plants manufacturing, processing, and using MBT and its derivatives, and to terrestrial populations in areas accumulating a high-density of rubber dust, or in areas receiving waste rubber, i.e., discarded tires (Ref. 19). Using the ENPART environmental partitioning model, the Agency estimated the mass distribution of MBT in the air, water (including sediments), and soil would be 0.0003, 9.9933, and 0.0064, respectively (Ref. 25). The Agency has received CBI release data submitted by the manufacturers of MBT.

MBT (0.03 mg/l) and benzothiazole (0.06 mg/l) have been found in tire-manufacturing waste water effluent (Ref. 18). MBT was also detected in an aerated lagoon at a synthetic rubber plant (Ref. 26) and in the effluent from a waste dump (0.03 mg/l), where MBT was thought to have been disposed (Ref 27). MBT was found to be the principal contaminant in waste water from the production of MBT derivatives (Ref. 28).

Mean concentrations of MBT in 18 surface water samples were all below the detection limit of 10 ppb (Ref. 29). These water bodies were generally large and in many cases appear to be far removed from potential industrial contamination sources.

Based on information supplied by CMA (Refs. 29 and 32) and the 1983 sales volume of MBT (5,958,000 lbs), EPA estimates that 1,000,000 pounds of MBT are released to the environment annually from the manufacturing, processing, use, and disposal of MBT. It has been estimated that a tire plant producing 25,000 steel belted radial tires per day would release 156 lbs of MBT and 312 lbs of benzothiazole annually (Ref. 18).

CMA prepared a "worst case" aquatic exposure estimate (Ref. 29). The model conclusions were concentrations of 0.545 ppb for rivers with a retention time of 7 days and 0.015 ppb for lakes with a 300-day retention time.

Using the CBI production and release information submitted by the manufacturers of MBT, EPA estimated concentrations of MBT in the air and water near MBT manufacturing sites (Ref. 30). The atmospheric concentration estimates ranged from 15 to 429 parts per trillion and were based on the assumption of 250 operating days per year and an atmospheric half-life for MBT of one day (Ref. 30). Surface water concentrations ranged from 2.90 to 385 ppb and were based on releases over 365 days per year from treatment facilities with no removal of the chemical by adsorption or other processes. Environmental processes including oxidation and photolysis were accounted for; however, it was assumed that MBT does not biodegrade in surface waters (Ref. 30).

Tire wear results in approximately 1.2 billion pounds of rubber dust in the United States each year (Ref. 31). If the initial tire rubber formula contains about 1 percent accelerator as a theoretical maximum, roughly 12 million pounds of vulcanization accelerator products could reach the air and soil adjacent to highways each year (Ref. 1). Since accelerators do degrade during vulcanization, the 12 million pounds would not be entirely MBT but more likely would include degradation products such as benzothiazole. CMA has estimated that 19,200 pounds of MBT could enter the aquatic environment for tire dust. This is based on the estimate that 1.2 billion pounds of tire dust are deposited along U.S. highways each year (Ref. 31) and that 0.0016 percent of the material extracted from rubber dust was MBT (Ref. 32). This estimate appears to be low because the percent of MBT extracted from the rubber was only based on a 7-day study and does not reflect annual release.

E. Health Effects

1. *Metabolism.* The Agency has reviewed several metabolism studies and has found them insufficient to predict the metabolism of MBT. Absorption of MBT from the gastrointestinal tract is indicated by the occurrence of toxic effects in animals and humans that were exposed by the oral route (Ref. 33). The percutaneous absorption of MBT in aqueous solution has also been demonstrated (Ref. 34). Storage of MBT could not be demonstrated in the liver, kidney, or spleen following oral administration; the extent of storage in fat or other tissues was not ascertained (Ref. 35).

Experiments conducted by Nagamatsu et al. (Ref. 34) showed that 6 hours after dosing, 90 percent of radioactive ^{14}C-MBT was excreted in the urine as the glucuronide and sulfate conjugates of MBT; 7.8 percent of the urine radioactivity represented untransformed MBT.

Colucci has proposed metabolic pathways for MBT in the rat, rabbit, and dog (Ref. 33).

2. *Acute toxicity.* The Agency has reviewed several acute toxicity studies for MBT and has found these studies adequate to predict the acute toxicity. These acute toxicity studies of MBT resulted in oral LD_{50} values ranging from 2,000 to 3,000 mg/kg for rats, mice, and guinea pigs (Ref. 36, 37, and 38). Intraperitoneal administration of MBT to rats, mice and guinea pigs resulted in LD_{50} values ranging from 200 to 400 mg/kg (Ref. 37 and 38).

It is well established that MBT, particularly as a component in rubber products, is one of the most common human contact allergens (Ref. 54 through 58).

3. *Subchronic toxicity.* The Agency has reviewed several subchronic toxicity studies for MBT and has found these studies adequate to predict the subchronic toxicity of MBT. The subchronic administration of MBT to male mice by daily intraperitoneal injections for 1 week at doses of 100 and 55 mg/kg (corresponding to one-fourth and one-eighth the LD_{50}, respectively) revealed extensive liver necrosis in the high-dosage group (Ref. 36). No histopathology was done on the 55 mg/kg dose group. In a related experiment the sleep time in a hexabarbital narcosis study was significantly increased in the high-dosage group, thus indicating functional damage to the liver (Ref. 36).

The results of a subchronic test in which mice and rats were exposed to MBT to determine the maximum tolerated dose for use in a chronic test have been reported to the Agency. MBT was administered by gavage to mice at doses of 94, 188, 375, 750, and 1,500 mg/kg body weight, and to rats at 188, 375,

750, 1,500, and 3,000 mg/kg body weight. Chemical related mortalities occurred at 750 and 1,500 mg/kg for female and male mice and female rats, respectively. Weight gain decrements were found to be dose-level related for both species. Distal convoluted tubular epithelial necrosis of the kidney was identified as a target organ lesion for both sexes of the rat at the 3,000 mg/kg level. The maximum tolerated dose for rats and mice was established, at 375 mg/kg body weight (Ref. 39).

4. *Chronic toxicity and oncogenicity.* MBT is the subject of a carcinogenesis study at the National Toxicology Program (NTP). In this study, now in the histopathology phase, rats and mice were exposed to MBT by gavage.

5. *Developmental and reproductive toxicity.* The Agency has reviewed several teratology and reproduction studies and has found them to be inadequate to reasonably predict the developmental and reproductive toxicity of MBT. Several of these studies were designed as screening studies; others were abstracted from Russian literature and details necessary for a thorough review were not available.

The teratogenic potential of intraperitoneally-injected MBT was assessed as part of a NIOSH-sponsored screening study (Ref. 40). Young adult female Sprague-Dawley rats were administered daily injections of 200 mg/kg of MBT in corn-oil on days 1 through 15 of gestation. Examinations conducted on day 21 of gestation showed no evidence of maternal toxicity, fetal toxicity, or teratogenesis. This study is of limited value because it was designed as a screening study and only small group sizes were used.

A more in-depth screening program has been conducted to evaluate the teratogenic potential of MBT. This study included daily subcutaneous injections to three strains of mice on gestation days 6 through 14 for C57 and C3H mice and on gestation days 6 through 15 for AKR mice. The dosages were 464 mg/kg/day (C57, AKR, and C3H mice) and 300 mg/kg/day (C3H mice). All doses were less than the MTD. The mice were sacrificed on the appropriate day of gestation, at which time maternal toxicity and fetotoxicity were assessed. Results of the study show that there was an increased incidence of abnormal fetuses at 464 mg/kg in the C3H and C57 strains. The significance of these findings is unclear, however, because the data are inconsistent and incidences of specific abnormalities were not reported. There was also evidence of fetal and maternal toxicity in the 464 mg/kg C3H mice, increased maternal liver weights in all groups except C3H mice, and a lack of additional dose levels for evaluation of dose-response relationships (Ref. 41).

In a Russian study MBT and other MBT derivatives were administered to albino rats to evaluate the teratogenic effects. Albino rats dosed with MBT at 20 mg/kg on days 4 and 11 of pregnancy showed a significant increase in embryonic mortality. Criteria for statistical significance and data supporting the decrease in fetal body weight were not reported (Ref. 42).

The teratogenicity of several of the mercaptobenzothiazoles was evaluated in the chicken embryo (Refs. 43 and 44). Technical-grade MBT at a concentration of 0.10 to 2.0 umol/egg was injected in an acetone vehicle onto the heart of 3-day-old embryos. Two types of eye defects were found frequently in the malformed embryos, as well as defects of the neck and back and open coelom. Incidences of specific malformations were not tabulated in this review.

6. *Mutagenicity.* The genotoxic potential of MBT and several of its derivatives has been evaluated in studies with bacteria, mammalian cells, intact mammals, and *Drosophila.* The review of these studies has led the Agency to conclude that there is adequate information to reasonably predict the gene mutation potential of MBT but inadequate information to predict the potential for MBT to induce chromosomal effects.

MBT has been reported to be nonmutagenic in the Ames *Salmonella typhimurium* reverse mutation assay when tested with strains TA1535 TA1537, TA1538 and/or TA100 (Refs. 45 through 47).

Several other gene mutation studies have been carried out with MBT. MBT does not induce mutations at the HGPRT locus in cultured Chinese Hamster Ovary (CHO) cells or in *Escherichia coli* (Refs. 48 and 49).

More recent studies suggest that MBT is not likely to be mutagenic in a mouse lymphoma assay (Ref. 50). A CMA-sponsored L5178Y mouse lymphoma assay showed a weak positive response (increase in mutant frequency at the TK locus) at MBT dose levels that were highly toxic. These assays were carried out with and without added rat liver S-9 activiation. The results of the assay indicate weak mutagenicity of MBT at doses that were highly toxic, i.e., causing relative growth rates of 20 percent or less. However, the elevated mutation frequencies may be attributable to a cytotoxic rather than a genotoxic effect.

The results of a micronucleus test showed that intraperitoneal administration of 300 mg/kg of MBT to male and female Swiss mice failed to cause an increase in micronucleated polychromatic erythrocytes in the bone marrow (Ref. 51).

The results of a dominant le[illegible]dy using albino rats indicate that M[illegible]ay induce genetic damage (Ref. 42). MBT was administered by gavage to female rats at a dose of 200 mg/kg on the first and third days of estrus, and to male rats twice at an interval of 3 days (time prior to mating not reported). Results obtained following sacrifice, on the 19th day of pregnancy, indicate mutagenic action. This interpretation is complicated by the unknown interval between male exposure and mating, exposure of the female during estrus, and an lack of a male-only exposure group.

7. *Neurotoxicity.* No data on the neurotoxic effects of MBT have been found in the literature.

F. Environmental Effects

Acute toxicity of MBT has been measured using fingerling rainbow trou (*Salmo gairdneri*). A flow-through system with measured concentrations yielded 24, 96, and 192 hour LC_{50} values of 1.14, 0.73, and 0.67 mg/l, respectively (Ref. 52). The toxicity of NaMBT using rainbow trout and bluegill sunfish (*Lepomis macrochirus*) was measured using acute static exposures and a 50-percent aqueous NaMBT formulation (Ref. 59). No mortalities were observed beyond 24 hours, leading the [illegible] to conclude that the test materia[illegible]ts potency after 24 hours. The calculated LC_{50} values for MaMBT at 96 hrs were 2.80 mg/l for trout and 13.3 mg/l for bluegills.

Static 96-hour LC_{50} values for MBT include 0.75 mg/l for rainbow trout, 1.5 mg/l for bluegills, and 11 mg/l for fathead minnows (*Pimephales promelas*). Comparable LC_{50} values for 50-percent NaMBT were 1.8 mg/l and [illegible] mg/l for rainbow trout and bluegills (Ref. 60).

A static acute toxicity assay of MBT and NaMBT with the invertebrate *Daphnia magna* yielded 24-hour and 48-hour EC_{50} values of 7.0 mg/l and 4.1 mg/l, respectively. The 24-hour and 48-hour EC_{50} values for NaMBT-50 percent we[illegible] 44 mg/l and 19 mg/l, respectively (Refs. 61 and 62).

Acute toxicity studies of MBT and NaMBT using the alga *Selanastrum capricornutum* have reported 96-hour EC_{50} values of 230 mg/l for MBT on chlorophyll and 250 mg/l for MBT on cell count. The EC_{50} value for 96-hr chlorophyll using 50 percent NaMBT [illegible] 0.4 mg/l and 0.3 mg/l for cell count. (Refs. 63 and 64).

MBT, MBTS and N-cyclohexyl-2-benzothiazole sulfenamide (CBS) have been shown to be toxic to the growth of soil microorganisms. The LD_{50} value for MBT was given as <0.1 percent, and the LD_{50} values for MBTS and CBS were 0.75 percent and 0.25 percent, respectively (Ref. 65). MBT derivatives are known to have bacteriocidal, bacteriostatic and fungicidal effects. The Agency finds that there are adequate data available to predict the acute toxicity to fish, aquatic invertebrates, and plants; however, the chronic toxicity data are inadequate.

G. Chemical Fate

MBT can enter the environment during production, processing, and disposal of MBT and rubber products. In general, MBT is nonvolatile and will tend to partition mainly to water rather than to soil and air. MBT has a relatively high water solubility (51 mg/l at pH5, 118 mg/l at pH7 and 900 mg/l at pH9), a low experimentally-derived vapor pressure (1.9×10^{-4} torr), and a measured log octanol/water partition coefficient of 2.42 (Ref. 2), which indicates that MBT will partition mainly to water. Because of MBT's moderate partition coefficient it is not expected to bioconcentrate significantly. A bioconcentration factor of 25 has been estimated (Ref. 29). Measured adsorption to soil or sediment appears to be only moderate (Ref. 66).

Under environmental conditions, MBT is not susceptible to hydrolysis. High pH is required to hydrolyze MBT. It has been demonstrated that MBT photolyzes in pure water and water containing dissolved humic acids (Ref. 67). However, no environmentally relevant photolysis rate data in aqueous media, and particularly in aquatic humic media, are available on MBT to determine its environmental fate.

Limited evidence of biodegradation is available. MBT is oxidized by mixed cultures and sludge microorganisms (Ref. 69). MBT was found to be degradation-resistant (less than 30 percent of theoretical BOD in 2 weeks) with activated sludge inoculum (Ref. 70). No degradation was seen after 30 days using a COD method, and only 2 percent of maximum CO_2 evolution was found indicating that MBT was essentially undegradable under the conditions of the experiment (Ref. 71). It has been reported that MBT, MBTS, and the MBT derivative N-cyclohexyl-2-benzothiazole sulfenamide (CBS) did not support the growth of soil microbes (Ref. 65).

The Agency has found that there are adequate chemical fate data available to predict the solubility, volatility, octanol/water partition coefficient, bioconcentration, and hydrolysis of MBT. The Agency has found a lack of data on the aquatic biodegradation and chemical mobility of MBT, and insufficient information to characterize the aqueous photolysis of MBT.

III. Findings

A. Environmental Effects and Chemical Fate

EPA is basing its proposed environmental effects and chemical fate testing for MBT on the authority of sections 4(a)(1) (A) and (B) of TSCA.

EPA has found that MBT is produced in substantial quantities. This finding takes into account TSCA section 8(a) information that was submitted by the manufacturers of MBT, the indirect production of MBT as a result of the breakdown of MBT-derived accelerators during vulcanization, and the 1983 sales volume of MBT, which was reported by the USITC to be 5,998,000 pounds. EPA also finds that there may be substantial release of MBT to the environment. This finding considers TSCA section 8(a) release data submitted by the manufacturers of MBT, release from processing, release from disposal, release from coolants, and EPA's estimate that 1,000,000 pounds of MBT may be lost to the environment annually through both direct and indirect discharges. MBT release is also expected to occur as a result of the break-down of MBT-derived accelerators in discarded rubber products.

EPA has concluded that the manufacture, processing, use, and disposal of MBT may present an unreasonable risk of injury to organisms in the aquatic environment. EPA is basing this finding on acute toxicity data that are less than 1,000-fold greater than the predicted environmental concentration. The criterion of 1,000x is the uncertainty factor used to relate acute toxicity and predicted environmental concentrations. It is a product of three uncertainty factors: (1) A factor for extrapolating from an insensitive to sensitive species for acute toxicity, (2) a factor for extrapolating from acute to chronic toxicity, and (3) a factor for extrapolating from chronic laboratory toxicity to field or *in situ* toxicity. The existing acute toxicity data show a decrease in LC_{50} values over time. These data indicate that chronic effects may present an unreasonable risk at considerably lower concentrations. EPA believes that chronic effects may occur at the predicted environmental concentrations.

EPA has found no data on the chronic effects of MBT on fish and aquatic invertebrates. EPA has also concluded that the data are inadequate to reasonably predict the persistence and mobility of MBT once it is released into the environment. Therefore, EPA has concluded that available data are inadequate to reasonably determine or predict the chronic effects on fish and aquatic invertebrates from the manufacture, processing, use, and disposal of MBT, nor can the data predict the persistence and mobility of MBT released from such activities. EPA had concluded that testing is necessary to develop such data.

The Agency finds that sufficient data are available in the published literature to satisfy the ITC's recommendation that the dissociation constant be determined. Two experimentally-derived values have been found in the literature and indicate that the dissociation constant is 8.93 (Ref. 29).

After reviewing and evaluating the existing aquatic toxicity data for MBT, EPA has determined that there are sufficient data available to reasonably predict the acute toxicity of MBT to fish, aquatic invertebrates, and plants. MBT has been shown to exert a high acute toxicity in rainbow trout with a 96-hour LC_{50} of 0.73 mg/l. *Daphinia magna* has been shown to have a 48-hour LC_{50} value of 4.1 mg/l, and *Selenastrum capricornutum* has a 96-hour EC_{50} of 230 mg/l. Therefore, EPA is not requiring any additional acute toxicity tests at this time. Should the existing data and the chronic testing proposed in the rule provide results indicating a high priority for control of aquatic concentrations of MBT under the Clean Water Act, EPA may at that time propose additional acute and/or chronic testing to establish water quality criteria pursuant to Section 304(a)(1) of the Clean Water Act.

The Agency has no evidence of substantial exposure of terrestrial plants along the roadside to MBT from tire dust; therefore, the Agency at this time is not proposing any acute or chronic toxicity testing for terrestrial plants.

B. Human Health Effects

EPA is basing its proposed health effects testing for MBT on the authority of TSCA section 4(a)(1)(B). EPA finds that MBT is produced in substantial quantities. EPA also finds that there may be substantial human exposure to MBT. The National Occupational Hazard Survey (NOHS) conducted in 1972–1974 estimates that as many as 558,693 people in the chemical industry may be exposed to MBT. The National Occupational Exposure Survey (NOES) data base estimates that 2,398 workers

(of whom 119 are female) are exposed to MBT. A substantial number of consumers also may be exposed to MBT as a result of its presence in finished rubber products.

EPA finds that there is or will be sufficient data available to reasonably determine or predict the acute effects, chronic effects, oncogenic effects, and gene mutation effects of exposure to MBT. EPA finds that there are insufficient data available to reasonably determine or predict the effects of the manufacture, processing, use and disposal of MBT in the areas of metabolism, developmental toxicity, reproductive toxicity, chromosomal aberrations, and neurotoxicity. EPA finds that testing of MBT is necessary to develop such data.

IV. Proposed Rule

A. Proposed Testing and Test Standards

The Agency is proposing that testing be conducted in accordance with specific test guidelines set forth in Title 40 of the Code of Federal Regulations as enumerated below. Test methods under new Parts 796, 797, and 798 were published in the Federal Register of September 27, 1985 (50 FR 39252).

On the basis of the findings presented above for chemical fate testing, the Agency is proposing that MBT be tested for: (1) Biodegradation using the test specified in § 796.3100 of this chapter; (2) indirect photolysis screening using the test specified in § 796.3765 of this chapter, as appears in the proposed rule for phenylene-diamines, a copy of which is in the docket of this rule for MBT; and (3) chemical mobility using the test specified in § 796.2750 of this chapter.

On the basis of the findings presented above for environmental effects testing, the Agency is proposing that chronic toxicity testing of MBT shall be conducted on (1) rainbow trout (*Salmo gairdneri*) using the test specified in § 797.1600 of this chapter; and (2) *Daphnia magna* using the test specified in § 797.1330 of this chapter.

On the basis of the findings presented above for health effects testing, the Agency is proposing that MBT be tested for: (1) Oral and dermal pharmacokinetics using the test specified in § 798.7470 of this chapter; (2) developmental toxicity using the test specified § 798.4900 of this chapter; (3) reproductive toxicity using the test specified in § 798.4700 of this chapter; and (4) neurotoxicity using the tests specified in §§ 798.6050, 798.6200, and 798.6400 of this chapter.

To assess the potential for MBT to cause chromosomal aberrations, the Agency is proposing that *in vitro* cytogenetic assays be conducted on MBT as specified in § 798.5375 of this chapter. Unless the results of the *in vitro* test are negative, a dominant-lethal assay will be required using the procedures specified in § 798.5450 of this chapter. A positive result in the dominant-lethal assay will trigger a heritable translocation assay using the procedures specified in § 798.5460 of this chapter. If the *in vitro* cytogenetics assay is negative, an *in vivo* bone marrow assay using procedures specified in § 798.5385 of this chapter will be required. Should the *in vivo* bone marrow test results prove negative, no further chromosomal aberrations testing would be required. A non-negative result in the *in vivo* bone marrow test would trigger the dominant-lethal assay. Again, if the dominant-lethal test is positive a heritable translocation assay shall be conducted. If the dominant-lethal test is negative, no further chromosomal aberrations testing will be required for MBT.

If the results of the dominant-lethal assay are positive, EPA will hold a public program review prior to initiating the heritable translocation assay. Public participation in this program review will be in the form of written public comments or a public meeting. Request for public comments or notification of a public meeting will be published in the Federal Register. Should EPA determine, based on the available weight of evidence, that proceeding to the heritable translocation test is no longer warranted, the Agency would propose to repeal that test requirement and, after public comment, issue a final amendment to rescind the requirement.

For a more detailed discussion concerning mutagenicity-tiered testing and public program review procedures see EPA's final test rule for the C9 aromatic hydrocarbon fraction published in the Federal Register of May 17, 1985 (50 FR 20662).

The Agency is proposing that the above-referenced TSCA chemical fate, environmental effects, and health effects test guidelines be employed as the test standards for the purposes of the proposed tests for MBT.

The TSCA test guidelines for chemical fate, aquatic toxicity, and health effect testing specify generally accepted minimal conditions for determining the fate, aquatic toxicities, and health effects for substances like MBT to which humans and the environment are expected to be exposed. The Agency's review of the TSCA Test Guidelines, which occurs on a yearly basis according to the process described at 47 FR 41857 (September 22, 1982), has found no reason to conclude that these protocols need to be modified significantly.

EPA intends to propose shortly a separate Federal Register notice on revisions to these TSCA Test Guidelines to provide more explicit guidance on the necessary minimum elements for each study. In addition, these revisions will avoid repetitive chemical-by-chemical changes to the guidelines in their adoption as test standards for chemical-specific test rules. EPA is proposing that these modifications be adopted in the test standards for MBT.

B. Test Substance

EPA is proposing that MBT of at least 98 percent purity be used as the test substance. EPA has specified a relatively pure substance for testing because the Agency is interested in evaluating the effects attributable to MBT itself. MBT of at least 98 percent purity is commerically available.

C. Persons Required to Test

Section 4(b)(3)(B) specifies that the activities for which the Agency makes section 4(a) findings (manufacture, processing, distribution, use, and/or disposal) determine who bears the responsibility for testing. Manufacturers are required to test if the findings are based on manufacturing ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors are required to test if the findings are based on processing. Both manufacturers and processors are required to test if the findings are based on distribution, use, or disposal.

Because EPA has found that there are insufficient data and experience to reasonably determine or predict the effects of the manufacture, processing, use, and disposal of MBT on human health or the environment, EPA is proposing that persons who manufacture and/or process, or who intend to manufacture and/or process, MBT at any time from the effective date of the final test rule to the end of the reimbursement period be subject to the testing requirements contained in this proposed rule. The end of the reimbursement period for this rule will be 5 years after the last final report is submitted.

Because TSCA contains provisions to avoid duplicative testing, not every person subject to this rule must individually conduct testing. Section 4(b)(3)(A) of TSCA provides that EPA may permit two or more manufacturers or processors who are subject to the rule to designate one such person or a qualified third person to conduct the tests and submit data on their behalf.

Section 4(c) provides that any person required to test may apply to EPA for an exemption from the requirement. EPA promulgated procedures for applying for TSCA section 4(c) exemptions in 40 CFR Part 790.

When both manufacturers and processors are subject to a test rule, EPA expects that manufacturers will conduct the testing and that processors will ordinarily be exempted from testing. As described in 40 CFR Part 790, processors will be granted an exemption automatically without filing applications if manufacturers perform all of the required testing. Manufacturers are required to submit either a letter of intent to perform testing or an exemption application within 30 days after the effective date of the test rule.

EPA is not proposing to require the submission of equivalence data as a condition for exemption from the proposed testing for MBT. As noted in Unit IV.B above, EPA is interested in evaluating the effects attributable to MBT itself and has specified a highly pure substance for testing.

Manufacturers and processors subject to this test rule must comply with the test rule development and exemption procedures in 40 CFR Part 790 for single-phase rulemaking.

D. Reporting Requirements

EPA is proposing that all data developed under this rule be reported in accordance with its TSCA Good Laboratory Practice (GLP) standards, which appear in 40 CFR Part 792.

In accordance with 40 CFR Part 790 under single-phase rulemaking procedures, test sponsors are required to submit individual study plans at least 30 days prior to the initiation of each study.

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. The Agency is proposing specific reporting requirements for each of the proposed tests as follows:

1. The photolysis, chemical mobility, pharmacokinetics, developmental toxicity, neurotoxicity, and chronic aquatic vertebrate and invertebrate toxicity tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final test rule. Quarterly progress reports shall be required.

2. The reproductive toxicity testing shall be completed and the final results submitted to the Agency within 29 months of the effective date of the final test rule. Quarterly progress reports shall be required.

3. The chromosomal aberration tests for MBT shall be completed and the final results submitted to the Agency after the effective date of the final rule as follows: *in vitro* cytogenetics, 12 months; *in vivo* cytogenetics (bone marrow cytogenetics), 12 months; dominant lethal assay, 24 months; heritable translocation assay, 48 months. There will be a public program review before the heritable translocation test is conducted. Quarterly progress reports are required for all mutagenicity tests.

TSCA section 14(b) governs Agency disclosure of all test data submitted pursuant to section 4 of TSCA. Upon receipt of data required by this rule, the Agency will publish a notice of receipt in the **Federal Register** as required by section 4(d).

Persons who export a chemical substance or mixture subject to a section 4 test rule are subject to the export reporting requirements of section 12(b) of TSCA. Final regulations interpreting the requirements of section 12(b) are in 40 CFR Part 707 (45 FR 82844; December 16, 1980). In brief, as of the effective date of the final test rule, an exporter of MBT must report to EPA the first annual export or intended export of MBT to any one country. EPA will notify the foreign country concerning the test rule for the chemical.

E. Enforcement Provisions

The Agency considers failure to comply with any aspect of a section 4 rule to be a violation of section 15 of TSCA. Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to: (1) Establish or maintain records; (2) submit reports, notices, or other information; or (3) permit access to or copying of records required by the Act or any regulation or rule issued under TSCA.

Additionally, TSCA section 15(4) makes it unlawful for any person to fail or refuse to permit entry or inspection as required by section 11. Section 11 applies to any "establishment, facility, or other premises in which chemical substances or mixtures are manufactured, processed, stored, or held before or after their distribution in commerce * * *." The Agency considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory inspections and data audits will be conducted periodically in accordance with the authority and procedures outlined in TSCA section 11 by duly designated representatives of the EPA for the purpose of determining compliance with any final rule for MBT. These inspections may be conducted for purposes which include verification that testing has begun, that schedules are being met, that reports accurately reflect the underlying raw data and interpretations and evaluations, and to determine compliance with TSCA GLP standards and the test standards established in the rule.

EPA's authority to inspect a testing facility also derives from section 4(b)(1) of the TSCA, which directs EPA to promulgate standards for the development of test data. These standards are defined in section 3(12)(B) of TSCA to include those requirements necessary to assure that data developed under testing rules are reliable and adequate, and to include such other requirements as are necessary to provide such assurance. The Agency maintains that laboratory inspections are necessary to provide this assurance.

Violators of TSCA are subject to criminal and civil liability. Persons who submit materially misleading or false information in connection with the requirement of any provision of this rule may be subject to penalties which may be calculated as if they never submitted their data. Under the penalty provision of section 16 of TSCA, any person who violates section 15 could be subject to a civil penalty of up to $25,000 for each violation with each day of operation in violation constituting a separate violation. This provision would be applicable primarily to manufacturers or processors that fail to submit a letter of intent or an exemption request and that continue manufacturing or processing after the deadlines for such submissions. Knowing or willful violations could lead to the imposition of criminal penalties of up to $25,000 for each day of violation and imprisonment for up to 1 year. In determining the amount of penalty, EPA will take into account the seriousness of the violation and the degree of culpability of the violator as well as all the other factors listed in section 16. Other remedies are available to EPA under section 17 of TSCA, such as seeking an injunction to restrain violations of TSCA section 4.

Individuals as well as corporations could be subject to enforcement actions. Section 15 and 16 of TSCA apply to "any person" who violates various provisions of TSCA. EPA may, at its discretion, proceed against individuals as well as companies. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.C. 1001.

V. Issues

This proposed rule identifies various test guidelines as test standards for health and environmental effects testing and chemical fate testing of MBT. The Agency is soliciting comments as to whether these health and environmental effects and chemical fate test guidelines are appropriate and applicable for the testing of MBT. Also regarding the testing of MBT, the Agency requests comments on the adequacy of this testing and the reporting times for the identified health and environmental effects and chemical fate tests.

VI. Economic Analysis of Proposed Rule

To assess the economic impact of this rule, EPA has prepared an economic analysis that evaluates the potential for significant economic impacts on the industry as a result of the required testing. The economic analysis estimates the costs of conducting the required testing and evaluates the potential for significant adverse economic impact as a result of these test costs by examining four market characteristics of MBT: (1) Price sensitivity of demand, (2) industry cost characteristics, (3) industry structure, and (4) market expectations.

Total testing costs for the proposed rule for MBT are estimated to range from $246,785 to $596,630. The annualized test costs (using a cost of capital of 25 percent over a period of 15 years) range from $83,946 to $154,858. Based on an estimated 1984 production volume of 47.3 million pounds (Ref. 24), the unit test costs range from 0.001 to 0.003 dollar per pound. Relative to a current list price of $1.55 per pound for MBT, these costs are equivalent to 0.09 to 0.21 percent of price.

Based on these costs and the market characteristics of MBT, the economic analysis indicates that the potential for significant adverse economic impact as a result of this test rule is low. This conclusion is based on the following observations:

1. The annual unit cost of the testing required in this rule is very low;
2. Demand for MBT appears relatively inelastic due to its dominant use as an intermediate in the manufacture of the disulfide, salts, and sulfenamides of MBT; and
3. The market expectations of MBT are optimistic.

VII. Availability of Test Facilities and Personnel

Section 4(b)(1) of TSCA requires EPA to consider "the reasonably foreseeable availability of the facilities and personnel needed to perform the testing required under the rule." Therefore, EPA conducted a study to assess the availability of test facilities and personnel to handle the additional demand for testing services created by section 4 test rules. Copies of the study, Chemical Testing Industry: Profile of Toxicological Testing, can be obtained through the National Technical Information Service (NTIS), Springfield, VA (PB 82-140773). On the basis of this study, the Agency believes that there will be available test facilities and personnel to perform the testing in this proposed rule.

VIII. Public Meetings

If persons indicate to EPA that they wish to present oral comments on this proposed rule to EPA officials who are directly responsible for developing the rule and supporting analyses, EPA will hold a public meeting subsequent to the close of the public comment period in Washington, D.C. Persons who wish to attend or to present comments at the meeting should call the TSCA Assistance Office (TAO): Toll Free: (800-424-9065); in Washington, D.C.: (554-1404); Outside the U.S.A.: (Operator—202-554-1404), by December 23, 1985. A meeting will not be held if members of the public do not indicate that they wish to make oral presentations. While the meeting will be open to the public, active participation will be limited to those persons who arranged to present comments and to designated EPA participants. Attendees should call the TAO before making travel plans to verify whether a meeting will be held.

Should a meeting be held, the Agency will transcribe the meeting and include the written transcript in the public record. Participants are invited, but not required, to submit copies of their statements prior to or on the day of the meeting. All such written materials will become part of EPA's record for this rulemaking.

IX. Public Record

EPA has established a record for this rulemaking, (docket number OPTS-42073). This record contains the basic information considered by the Agency in developing this proposal and appropriate Federal Register notices. The Agency will supplement this record with additional relevant information as it is received.

This record includes the following information:

A. Supporting Documentation

(1) Federal Register notices pertaining to this rule consisting of:

(a) Notice containing the ITC designation of MBT to the Priority List.

(b) Rules requiring TSCA section 8(a) and (d) reporting on MBT.

(c) Notice containing the TSCA test guidelines cited as test standards for rule.

(2) Support document consisting economic analysis.

(3) Communications before proposal consisting of:

(a) Written public comments and letters.

(b) Contact reports of telephone conversations.

(c) Meeting summaries.

(4) Reports—published and unpublished factual materials.

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Confidential Business Information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection in the OPTS Reading Rm. E-107, 401 M St., SW., Washington, D.C., from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

X. Other Regulatory Requirements

A. Executive Order 12291

Under Executive Order 12291, EPA must judge whether a regulation is "Major" and therefore subject to the requirement of a Regulatory Inpact Analysis. EPA has determined that this test rule is not major because it does not meet any of the criteria set forth in section 1(b) of the Order, i.e., it will not have an annual effect on the economy of at least $100 million, will not cause a major increase in prices, and will not have a significant adverse effect on competition or the ability of U.S. enterprises to compete with foreign enterprises.

This proposed regulation was submitted to the Office of Management and Budget (OMB) for review as required by Executive Order 12291. Any comments from OMB to EPA, and EPA response to those comments, are included in the rulemaking record.

B. Regulatory Flexibility Act

Under the Regulatory Fexibility Act (15 U.S.C.601 *et seq.*, Pub. L.96-354, September 19, 1980), EPA is certifying that this test rule, if promulated, will not have a significant impact on a substantial number of small businesses because: (1) They are not expected to perform testing themselves, or to participate in the organization of the testing effort; (2) they will experience only very minor costs, if any, in securing exemption from testing requirements; and (3) they are unlikely to be affected by reimbursement requirements.

C. Paperwork Reduction Act

The information collection requirements contained in this rule have been approved by the Office of Management and Budget (OMB) under the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 *et seq.*, and have been assigned OMB number 2070-0033. Comments on these requirements should be submitted to the Office of Information and Regulatory Affairs of OMB marked "Attention: Desk Officer for EPA." The final rule package will respond to any OMB or public comments of the information collection requirements.

List of Subjects in 40 CFR Parts 798 and 799

Testing, Environmental protection, Hazardous substances, Chemicals, Recordkeeping and recording requirements.

Dated: October 24, 1985.

J. S. Moore,

Assistant Administrator for Pesticides and Toxic Substances.

Therefore, it is proposed that Subchapter R of Chapter I of Title 40 of the Code of Federal Regulations be amended as follows:

PART 798—[AMENDED]

1. Part 798 is amended as follows:

a. The authority citation continues to read as follows:

Authority: 15 U.S.C. 2903.

b. New § 798.7470 is added to read as follows:

§ 798.7470 Oral and dermal pharmacokinetics.

(a) *Purpose.* The purpose of these studies is to:

(1) Determine the bioavailability of the test substance after dermal or oral administration;

(2) Ascertain whether the metabolites of the test substance are similar after dermal and oral administration; and

(3) Examine the effects of a repeated dosing regimen on the metabolism of the test substance.

(b) *Definitions.* (1) Pharmacokinetics is the study of the kinetics of absorption, distribution, metabolism, and excretion of the test chemical in an animal.

(2) Bioavailability refers to the rate and relative amount of administered test chemical which reaches the systemic circulation.

(c) *Test procedures*—(1) *Animal selection*—(i) *Species.* The rat shall be used for pharmacokinetics testing because it has been used extensively for absorption, metabolism, and toxicological studies. For dermal penetration studies, the female guinea pig shall also be used to provide additional information on dermal absorption.

(ii) *Animal strains.* Adult male and female Fischer 344 rats and female Hartley guinea pigs shall be use[illegible]7 to 9 weeks of age, the male rats weight 125 to 175 g and the fema[illegible]s 110 to 150 g. The female guinea pigs, 5 to 7 weeks old, shall weigh between 400 and 500 g. The animals should be purchased from a reputable dealer and shall be identified with ear tags upon arrival. The animals shall be selected at random for the testing groups. Animals showing signs of ill health shall not be used.

(iii) *Animal care.* (A) Animal care and housing should be in accordance with DHEW Publication No. (NIH)-7-23, 1978, "Guidelines for the Care and Use of Laboratory Animals."

(B) The animals should be housed in environmentally controlled rooms with 10 to 15 air changes per hour. The rooms shall be maintained at a temperture of 25 ± 2°C and humidity of 50 ± 10 percent with a 12-hour light/dark cycle per day. The rats shall be kept in a quarantine facility for at least 7 days prior to use.

(C) During the acclimatization period, the rats and guinea pigs should be housed in suitable cages on hardwood chip bedding. All animals shall be provided with certified feed and tap

water *ad libitum*. The guinea pig diet shall be supplemented with adequate amounts of ascorbic acid in the drinking water.

(2) *Administration of test substance*—(i) *Test compound.* These studies require the use of both nonradioactive test substance and radio-labeled test substance.

(ii) *Dosage and treatment*—(A) Two doses shall be used in the study, a "low" dose and a "high" dose. When administered orally, the "high" dose level should ideally induce some overt toxicity, such as weight loss. The "low" dose level should not induce observable effects attributable to the test substance. If feasible, the same "high" and "low" doses shall be administered orally and dermally.

(B) Oral dosing shall be accomplished by gavage or capsule.

(C) For dermal treatment, the doses shall be administered in a suitable vehicle and applied at a volume adequate to deliver the prescribed doses. The backs of the animals should be lightly shaved with an electric clipper 24 hours before treatment. The dose shall be applied with a micropipette on a specific area (2 cm^2 for rats, 5 cm for guinea, pigs, or at least 10% of body surface) of the intact shaven skin. The dosed areas shall be occluded with a suitable patch which is secured in place.

(iii) *Washing efficiency study.* Before initiation of the dermal absorption studies described in paragraphs (c)(2)(iv) (A)(*2*) and (B) of this section, an initial washing efficiency experiment shall be conducted to assess the removal of the applied test compound by washing the exposed skin area with soap and water or organic solvents. Four rats and 4 guinea pigs shall be lightly anesthetized and then the test compound applied at the low dose level to a specific area. After application (5 to 10 minutes), the areas shall be washed with soap and water (2 rats, 2 guinea pigs) or appropriate solvent (2 rats, 2 guinea pigs), then housed in individual cages for excreta collection. Urine and feces shall be collected at least once following dosing. The amount recovered shall be determined to assess efficacy of the test compound removal by washing of the skin.

(iv) *Determination of pharmacokinetics*—(A) *Rat studies.* Each experimental group shall contain at least four animals of each sex for a total of at least eight rats.

(*1*) *Oral studies. (i)* Group A shall be dosed once orally with the low dose of the test compound.

(*ii*) Group B shall be dosed once orally with the high dose of the test compound.

(*iii*) For the oral studies, the animals shall be placed in individual metabolic cages to facilitate collection of urine and feces at 8, 24, 48, 72 and 96 hours following administration. The cages shall be cleaned at each time period to collect any metabolites that might adhere to the metabolic cages.

(*2*) *Dermal studies. (i)* Group C shall be dosed once dermally with the low dose of the test compound.

(*ii*) Group D shall be dosed once dermally with the high dose of the test compound.

(*iii*) For the dermal studies, the test compound shall be kept on the skin for a minimum of 6 hours, or as determined by the adsorption properties of the compound. After application, each animal shall be placed in a separate metabolic cage for excreta collection. Urine and feces shall be collected at 8, 24, 48, 72, and 96 hours. At the time of removal of the patch, the occluded area shall be washed, with an appropriate solvent, to remove any test compound that may be on the skin surface. At the termination of the experiments, each animal shall be sacrificed and the exposed skin area removed. The skin (or an appropriate section) shall be solubilized and assayed for radioactivity to ascertain if the skin acts as a reservoir for the test compound.

(B) *Guinea pig studies.* The studies conducted on groups C and D as specified in paragraph (c)(2)(iv)(A) (*2*) of this section shall be repeated using female guinea pigs. Each group shall contain at least four female guinea pigs.

(v) *Repeated dosing study.* Group E (four rats, two of each sex) shall receive a series of single daily oral doses of nonradioactive test compound over a period of at least 14 days, followed at 24 hours after the last dose by a single oral dose of radio-labeled test compound. Each dose shall to be at the low dose level.

(3) *Observation of animals*— (i) *Bioavailability*—The levels of radioisotope shall be determined in whole blood, blood plasma or blood serum at 8, 24, 48, 72, and 96 hours after dosing rats as specified in paragraphs (c)(2)(iv)(A) and (v) of this section and guinea pigs as specified in paragraph (c)(2)(iv)(B) of this section. Four animals from each group shall be used for this purpose.

(ii) *Urinary and fecal excretion.* The quantities of radioisotope excreted in the urine and feces by rats dosed as specified in paragraphs (c)(2)(iv)(A) and (v) of this section and guinea pigs dosed as specified in paragraph (c)(2)(iv)(B) of this section shall be determined at 8, 24, 48, 72 and 96 hours after dosing, and if necessary, daily thereafter until at least 90 percent of the applied dose has been excreted or until 7 days after dosing (whichever occurs first). Four animals from each group shall be used for these analyses.

(iii) *Biotransformation after oral and dermal dosing.* Appropriate qualitative and quantitative methods shall be used to assay urine and fecale speciments collected from rats dosed as specified in paragraph (c)(2)(iv)(A) of this section. Efforts shall be made to identify any metabolite which comprises 10 percent or more of the dose excreted.

(iv) *Changes in biotransformation.* Appropriate qualitative and quantitative assay methodology shall be used to compare the composition of radio-labeled compounds in excreta (collected at 24 and 48 hours after dosing) from rats dosed as specified in paragraph (c)(2)(iv)(A)(*1*)(*i*) of this section with those in the excreta (collected at 24 and 48 hours after the radio-labeled dose) from rats in the repeated-dose study as specified in paragraph (c)(2)(v) of this section.

(d) *Data and reporting*—(1) *Treatment of results.* Data shall be summarized in tabular form.

(2) *Evaluation of results.* All observed results, quantitative or incidental, shall be evaluated by an appropriate statistical method.

(3) *Test report.* In addition to the reporting requirements as specified in the EPA Good Laboratory Practice Standards (Subpart J, Part 792 of this chapter) the following specific information shall be reported:

(i) Species and strains of laboratory animals;

(ii) Information on the degree (i.e., specific activity for a radiolabel) and site(s) of labeling of the test substance;

(iii) A full description of the sensitivity and precision of all procedures used to produce the data;

(iv) Percentage absorption of radio-labeled test compound after oral and dermal exposures to rats and fermal exposure to guinea pigs.

(v) Quantity of isotope, together with percent recovery of administered dose in feces, urine, blood and skin and skin washings (dermal study only for last two portions) of rats and quinea pigs.

(vi) Quantity and distribution of radio labeled test compound in various tissues, including bone, brain, fat, gonads, heart, kidney, liver, lung, muscle, spleen, and in residual carcass, of rats.

(vii) Biotransformation pathways and quantities of test substance and metabolites in excreta collected after administering single high and low oral and dermal doses to rats;

(viii) Biotransformation pathways and quantities of test substance and metabolites in excreta collected after administering repeated low doses of test compound to rats.

PART 799—[AMENDED]

2. 40 CFR Part 799 is amended as follows:

a. The authority citation continues to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

b. New § 799.2475 is added to read as follows:

§ 799.2475 Mercaptobenzothiazole.

(a) *Identification of test substance.* (1) 2-Mercaptobenzothiazole (CAS No. 149-30-4) (hereinafter "MBT") shall be tested in accordance with this section.

(2) MBT of at least 98 percent purity shall be used as the test substance.

(b) *Persons required to submit study plans, conduct tests, and submit data.* All persons who manufacture (import) or process MBT other than as an impurity after the effective date of this rule (December 19, 1985) to the end of the reimbursement period shall submit letters of intent to conduct testing or exemption applications, submit study plans, conduct tests, and submit data as specified in this section, Subpart A of this Part, and Part 790 for single-phase rulemaking.

(c) *Chemical fate testing*—(1) *Aerobic aquatic biodegradation*—(i) *Required testing.* Aerobic aquatic biodegradation tests shall be conducted with MBT in accordance with § 796.3100 of this chapter.

(ii) *Reporting requirements.* (A) The aerobic aquatic biodegradation tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(2) *Indirect photolysis—screening level test*—(i) *Required testing.* The indirect photolysis test shall be conducted with MBT in accordance with § 796.3765 of this chapter.

(ii) *Reporting requirements.* (A) The indirect photolysis test shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(3) *Chemical mobility*—(i) *Required testing.* The chemical mobility test shall be conducted with MBT in accordance with § 796.2750 of this chapter.

(ii) *Reporting requirements.* (A) The chemical mobility test shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(d) *Environmental effects testing*—(1) *Fish chronic toxicity*—(i) *Required testing.* (A) Chronic toxicity testing of MBT shall be conducted using rainbow trout (*Salmo gairdneri*) in accordance with § 797.1600 of this chapter and modifications specified in paragraph (d)(1)(i)(B) of this section.

(B) Modifications. The following modifications to § 797.1600 of this chapter for testing MBT are required.

(*1*) *Test substance measurement.* The requirement under § 797.1600(c)(6)(iv) is modified so that test substance concentration is also measured in the test substance delivery chamber prior to beginning, and during, the test.

(*2*) *pH.* The requirement under § 797.1600(d)(3) is modified so that a pH of 7 is recommended.

(*3*) *Reporting.* The requirement under § 797.1600(e) is modified to include an analysis of the stability of the stock solution for the duration of the test.

(ii) *Reporting requirements.* (A) The fish chronic toxicity tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(2) *Daphnid chronic toxicity*—(i) *Required testing.* (A) A daphnid chronic toxicity test shall be conducted with MBT using *Daphnia magna* in accordance with § 797.1330 of this chapter and modifications specified in paragraph (d)(2)(i)(B) of this section.

(B) Modifications. The following modifications to § 797.1330 of this chapter for testing MBT are required.

(*1*) *Test substance measurement.* The requirement under § 797.1330(d)(3)(ii)(B) is modified so that test substance concentration is also measured in the test substance delivery chamber prior to beginning, and during, the test.

(*2*) *pH.* The requirement under § 797.1330 (d)(3) is modified so that a pH of 7 is recommended.

(*3*) *Reporting.* The requirement under § 797.1330 (e) is modified to include an analysis of the stability of the stock solution for the duration of the test.

(ii) *Reporting requirements.* (A) Daphnid chronic toxicity tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(e) *Health effects testing*—(1) *Pharmacokinetic testing*—(i) *Required testing.* (A) Oral and dermal pharmacokinetic tests shall be conducted with MBT in accordance with § 798.7470 of this chapter.

(B) Modifications. (*1*) The requirement under § 798.7470(c)(2)(i) of this chapter for testing MBT is modified so that the compound is labeled with ^{14}C in the benzothiazole moiety.

(*2*) The requirement under § 798.7470(c)(2)(ii)(B) of this chapter for testing MBT is modified so that the oral dosing is accomplished by gavage after dissolving the MBT in a suitable vehicle.

(ii) *Reporting requirements.* (A) The pharmacokinetic tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress report shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(2) *Developmental toxicity testing*—(i) *Required testing.* Developmental toxicity tests shall be conducted with MBT in accordance with §798.4900 of this chapter.

(ii) *Reporting requirements.* (A) The developmental toxicity tests shall be completed and the final results submitted to the Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(3) *Reproductive toxicity*—(i) *Required testing.* Reproductive toxicity tests shall be conducted with MBT in accordance with § 798.4700 of this chapter.

(ii) *Reporting requirements.* (A) The reproductive tests shall be completed and the final results submitted to the agency within 29 months of the effective date of this final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(4) *Neurotoxicity*—(i) *Required testing.* Neurotoxicity tests shall be conducted with MBT in accordance with §§ 798.6050, 798.6200, and 798.6400 of this chapter.

(ii) *Reporting requirements.* (A) The neurotoxicity tests shall be completed and the final results submitted to the

Agency within 1 year of the effective date of the final rule.

(B) Progress reports shall be submitted to the Agency quarterly beginning 90 days after the effective date of the final rule.

(5) *Mutagenic effects—Chromosomal aberrations*—(i) *Required testing*—(A) *In vitro cytogenetics.* (*1*) An *in vitro* cytogenetics test shall be conducted with MBT in accordance with § 798.5375 of this chapter and modification specified in paragraph (e)(5)(i)(A)(*2*) of this section.

(*2*) **Modification.** The requirement under § 798.5375 (e)(3) of this chapter for testing MBT is modified so that the metabolic activation system is to be derived from Aroclor-induced rat liver S–9 preparation.

(B) *In vivo cytogenetics.* (*1*) An *in vivo* cytogenetics test shall be conducted with MBT in accordance with § 798.5385 of this chapter and modifications specified in paragraph (e)(5)(i)(B)(*2*) of this section if MBT produces a negative result in the *in vitro* cytogenetics test conducted pursuant to paragraph (e)(5)(i)(A) of this section and modification specified in paragraph (e)(5)(i)(A)(*2*) of this section.

(*2*) **Modifications** The following modifications to § 798.5385 of this chapter for testing MBT are required.

(*i*) The requirement under § 798.5385. (d)(3)(i) is modified so that only mice are used as test animals.

(*ii*) The requirement under § 798.5385 (d)(5)(iii) is modified so that the route of exposure for MBT is by oral gavage.

(C) A dominant-lethal assay shall be conducted with MBT in accordance with § 798.5450 of this chapter unless MBT produces negative results in both the *in vitro* and *in vivo* cytogenetics tests conducted pursuant to paragraphs (e)(5)(i)(A) and (B) of this section.

(D) A heritable translocation assay shall be conducted with MBT in accordance with the test guideline specified in § 798.5460 of this section if MBT produces a positive result in the dominant assay conducted pursuant to paragraph (e)(5)(i)(C) of this section.

(ii) *Reporting requirements.* (A) Mutagenic effects—chromosomal aberration tests with MBT shall be completed and the final results submitted to the Agency after the effective date of the rule as follows: *in vitro* cytogenetics, 12 months: *in vivo* cytogenetics, 12 months; dominant lethal assay, 24 months; heritable translocation assay, 48 months.

(B) Progress reports shall be submitted quarterly beginning 90 days from the effective date of the rule for all mutagenicity tests.

(Information collection requirements have been approved by the Office of Management and Budget under control number 2070–0033).

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